

REMARKS

Entry of the foregoing and further and favorable consideration of the subject application are respectfully requested.

As correctly stated in the Office Action, Claims 55-99 are pending in the present application. Claims 55-58, 61-79, 82, 85-94, and 97 stand rejected. Claims 59, 60, 80, 81, 83, 84, 95, 96, 98, and 99 stand withdrawn from consideration.

Claim 66 has been amended to delete the term "low molecular weight." No new matter has been added.

Request for Examiner Interview

Applicants respectfully request that the Examiner contact Applicants' undersigned representative prior to issuance of an Official Action, so that the presently claimed invention may be discussed in detail. However, if in light of the amendments and arguments contained in this response, the Examiner should deem the present claims under consideration allowable, an interview is considered unnecessary.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 55-58, 61-79, 82, 88-94, and 97 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite in the double inclusion of elements in the composition. Thus, the Examiner concludes that one skilled in the art would not be able to recognize the particular amounts of each recited in the claimed composition. This rejection is respectfully traversed.

Applicants respectfully submit that because the plasticizing agent is defined as an oil, ingredient c) would not overlap ingredient a), *i.e.*, the solvent. Additionally, the purpose of ingredient c) is clearly defined on page 8 of the specification and exemplified by fluid lanoline. More specifically, the oil to be used is an oil having the ability of plasticizing the viscosity enhancing agent and of reducing the viscosity of the carrier system to the desired level. Ingredient a) is used to dissolve the active agent. One skilled in the art would not confuse the oil of ingredient c) with the specific unsaturated fatty alcohols and alkylene glycol of ingredient a). Applicants respectfully submit that the differences between these two ingredients would be clear to one skilled in the art and thus, the claim language clearly sets forth the claimed invention. Accordingly, no amendment is believed to be necessary.

Claim 66 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner argues that the term "low" is not defined by the claim, nor by the specification. Without conceding the grounds of this rejection and solely in an effort to expedite prosecution, this language has been deleted from Claim 66, thereby mooted the rejection. Withdrawal of this rejection is thus respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 55-58, 61-79, 82, 85-94, and 97 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Yamada et al. (U.S. Patent 5,362,497) in view of Wang et al. (U.S. Patent No. 4,299,828) and Cooper et al. (U.S. Patent No. 4,552,872). The Examiner argues that Yamada et al. disclose a transdermal therapeutic composition

comprising a pharmaceutical active ingredient, a water-soluble absorption enhancer, a fat soluble absorption enhancer comprising fatty alcohol, and a lower alcohol ester of an aliphatic carboxylic acid. The Examiner admits that Yamada et al. do not expressly teach the particular formulation of the invention "which has corticosteroid as the active ingredient, and comprising unsaturated alcohols, lower alcohol ester of fatty acid, wax, and plasticizing oil with the particular percentage, or the particular form, stick, or the method of using the same." [See Official Action, pages 3-4]. However, the Examiner suggests that Cooper et al. disclose unsaturated alcohols are particularly useful in topical corticosteroid compositions and the inclusion of wax for stiffness. The Examiner further believes that Wang et al. disclose a corticosteroid stick formulation with wax. Thus, the Examiner surmises that one of "ordinary skill in the art would be motivated to modify the composition of Yamada et al. to make a corticosteroid topical composition ... employing oleyl alcohol as the fat soluble enhancer and propylene glycol as the water soluble enhancer with the particular amounts claimed herein." [See Official Action, page 4]. The Examiner argues that this is because both oleyl alcohol and propylene glycol are known to enhance the absorption of active ingredients. Finally, the Examiner asserts that the use of wax and plasticizer to render the final product certain properties is within the skill of artisan. This rejection is respectfully traversed.

In order to establish *prima facie* obviousness under 35 U.S.C. § 103, the cited reference or combination of references must teach or suggest every element of the claims. Moreover, there must be motivation, outside of Applicants' disclosure, to modify or combine the cited references. See M.P.E.P. 2143 *et seq.*

Applicants have highlighted the differences between the composition of Yamada et al. and the presently claimed invention in the Reply filed June 11, 2002 (see pages 4-5). Applicants respectfully submit that Yamada et al. disclose the benefits of separating two kinds of enhancers. In contrast, the presently claimed invention results in a homogeneous composition. Yamada et al. disclose the use of certain compounds as enhancers while the presently claimed invention utilizes the compounds for solvents. In the presently claimed invention, the particular combination of ingredients allows one to obtain a homogenous phase, without the use of the super water-absorbent resin relied upon by Yamada et al. If the compounds separate into a two-phase system, as occurs in the absence of the super water-absorbent resin, the intended solubility properties will change and the one will not obtain the presently claimed invention.

intended use is different

Further, Applicants respectfully maintain their position that Yamada et al. is irrelevant to the presently claimed invention and, in fact, teaches away from the presently claimed invention. Yamada et al. seek to avoid separation of a transdermal therapeutic composition, comprising a water-soluble and a lipid-soluble enhancer from an adhesive via the use of a water absorbent resin. See col. 2, lines 25-35. Yamada et al. explicitly state that the use of alkylene glycol and fatty acids or alcohols are incompatible (col. 1, lines 62-66). The presently claimed invention solves the incompatibility problem via specific mixtures of solvents to create a one-phase system while the solution to the problem in Yamada et al. is to utilize a superabsorbent polymer. This superabsorbent polymer is a critical element of the disclosure of Yamada et al. Applicants maintain that the skilled artisan would not obviously appreciate that enhanced homogeneity and penetration could be

generated by a formulation that does not contain adhesives and superabsorbing polymers such as those discussed by Yamada et al. Thus, there is no motivation to use a composition of Yamada et al. *sans* the adhesives and superabsorbing polymers because Yamada et al. specifically highlight the problems with such a composition. Finally, Applicants respectfully submit that the composition of Yamada et al. is intended for transdermal delivery of a therapeutic composition in order to produce the intended systemic effect (col. 1, lines 19-23), while Applicants' claimed invention is directed toward the local delivery of the therapeutic ingredient to the skin. *intended*

The Examiner argues that Cooper et al. teach the inclusion of a wax to impart the stiffness to the composition. Applicants acknowledge that Cooper discusses the use of wax in a composition. However, the Examiner ignores the express limitation of Cooper et al. on the amount of wax to be used in the composition. At col. 10, l. 40-42, Cooper et al. state that waxes "are capable of significantly interfering with the penetration enhancing abilities of the present invention." Thus, Cooper et al. conclude that, "while a certain level of such ingredients can be tolerated in a system which is otherwise particularly effective, in a preferred embodiment of the invention such ingredients are limited to less than about 10% and preferably less than 5%." (col. 10, l. 49-54).

In contrast, independent Claim 55 requires "b) a viscosity enhancing agent for imparting a solid consistency to the composition which comprises 15 to 55% by weight of a waxy substance." Thus, not only do Cooper et al. not disclose or suggest the specific limitations of the presently claimed invention, but Cooper et al. also expressly caution against using the very amounts the presently claimed invention advocates. Thus, Cooper et

al. cannot be considered to render the claimed invention obvious because it expressly teaches away from the particular limitations.

The Examiner argues that Applicants' previous remarks regarding the employment of hydrocarbons are irrelevant because all the elements employed in the claimed invention encompass alcohols, acids or esters which are not considered hydrocarbons. Applicants respectfully submit that this characterization of the presently claimed invention is incorrect. Claim 55 recites that the composition contains "b) a viscosity enhancing agent for imparting a solid consistency to the composition which comprises 15 to 55% by weight of a waxy substance." As can be seen from Claim 64, the waxy substance may be, inter alia, a natural or synthetic wax, which are hydrocarbons. Therefore, Applicants' comments are pertinent to the differences between Cooper et al. and the presently claimed invention.

The Examiner further argues that Wang et al. disclose that steroid containing stick compositions can be manufactured and that the active ingredient is preferably dissolved in the formulation. However, neither the disclosure of Wang et al. or of Cooper et al. render the present invention obvious. Wang et al. disclose a composition that the present specification demonstrates does not work in practice. The examples in the instant specification (as recited in independent claim 55) clearly show that if the composition contains less than 12% of alkylene glycol, the pharmaceutical activity of the formulation is very low. This is not disclosed or suggested by Wang et al. In fact, Wang et al. state that the propylene glycol (used as an antimicrobial but that also acts as a penetration enhancer) is preferably from about 2% to 10% by weight and optimally from about 3% to about 8%. Col. 3, lines 17-22. Wang et al. note that a concentration of 6% of propylene glycol kills

99.9% of bacteria. Col. 3, lines 24-29. Therefore, one skilled in the art would not be motivated to use higher concentration of propylene glycol (such as that found in the Yamada et al. publication) in a steroidal stick formulation based on the disclosure of Wang et al. Accordingly, the Wang et al. and Yamada et al. publications are incompatible.

Further, Wang et al. assert that waxes are preferably between about 10 to 40% and preferably about 15 to about 30% by weight. Col. 3, l. 13-16. As noted above, Cooper et al. expressly seek to avoid such high amounts of wax. Thus, the Cooper et al. and Wang et al. publications are incompatible and cannot be combined to render the presently claimed invention obvious. Applicants respectfully submit that the Examiner has attempted to combine references which expressly contradict the selection of certain components, without considering these express contradictions.

Assuming *arguendo* that these three publications could be combined, Applicants respectfully submit that one skilled in the art would not arrive at the presently claimed invention. If one modifies the Yamada composition, a system where the polymer stabilization of a two phase enhancer system is highlighted, by adding viscosity enhancers and employing oleic alcohol, one merely obtains a two-phase matrix thickened by both waxes and a polymeric emulsion stabilizer. The Examiner has provided no motivation to use the composition of Yamada et al. in the absence of the super water-absorbent polymer, the central focus of the Yamada et al. publication. Abiding by the disclosure of Cooper et al., one skilled in the art would believe that the presence of the waxes should be restricted to less than 10%. This resulting product will have very little, if anything, in common with the presently claimed invention.

Applicants respectfully submit that the three cited publications, Yamada et al., Cooper et al., and Wang et al., do not disclose all elements of the presently claimed invention, particularly the amounts of the different components of the composition. This is expressly acknowledged by the Examiner on page 4, lines 3-6, of the Official Action. Indeed, as Applicants have shown above, the cited publications are incompatible with each other and teach away from the presently claimed invention. Thus, none of the cited publications, either alone or in combination, render the presently claimed invention obvious. Accordingly, withdrawal of this rejection is respectfully requested.

*Amount
of particular
components*

Conclusions

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: February 6, 2003

Attachment to REPLY & AMENDMENT dated February 5, 2003

Marked-up Claim 66

66. (Amended) A composition as claimed in Claim 55, wherein the plasticizing oil is selected from [low molecular weight] aliphatic acids and alcohols.